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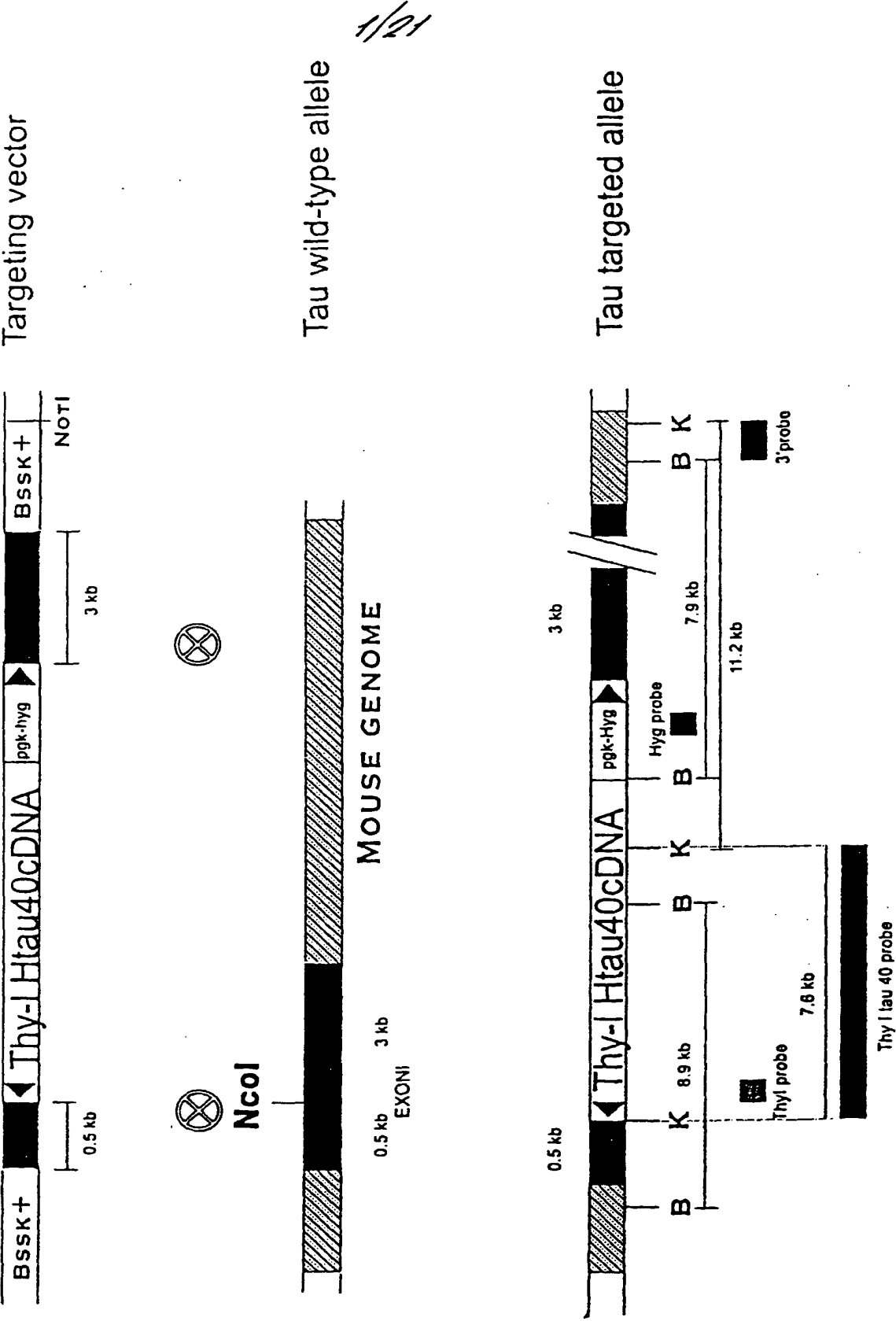
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(54) Title: TRANSGENIC ANIMALS AS MODELS FOR NEURODEGENERATIVE DISEASE

(57) Abstract: There is provided a nucleic acid vector comprising: (a) a nucleic acid sequence encoding a human Tau protein; (b) a sequence capable of directing expression of said human Tau protein in the nervous system of a non-human animal; and (c) a targeting sequence which facilitates integration of said vector into the genome of said animal so as to prevent expression of equivalent Tau protein or a related or equivalent protein from said animal in favour of said human Tau protein. A further aspect provides a nucleic acid vector comprising: (a) a nucleic acid sequence encoding a human protein capable of modulating human Tau protein; (b) a sequence capable of directing expression of said protein in the nervous system of said animal; and (c) a targeting sequence capable of facilitating integration of said vector into the genome of said animal optionally at a position corresponding to a sequence in said animal encoding an equivalent of said human protein so as to prevent expression of said equivalent sequence in favour of said human protein capable of modulating human Tau protein. The vectors are used to make a transgenic non-human animal by (a) introducing into an embryo cell of said animal one or more of a nucleic acid vector as described above; (b) introducing the embryo from step (a) into a female animal; (c) sustaining the female in step (b) until such time as the embryo has sufficiently developed and is borne from the female; and (d) sustaining the transgenic animal.

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FIG. 1.



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FIG. 2.

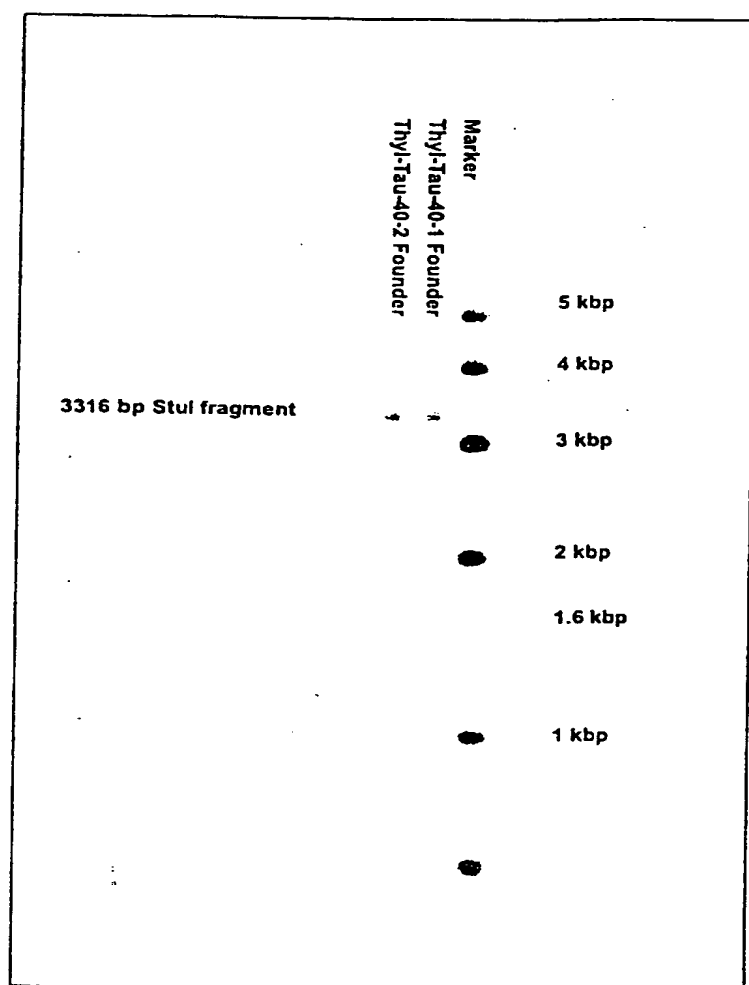
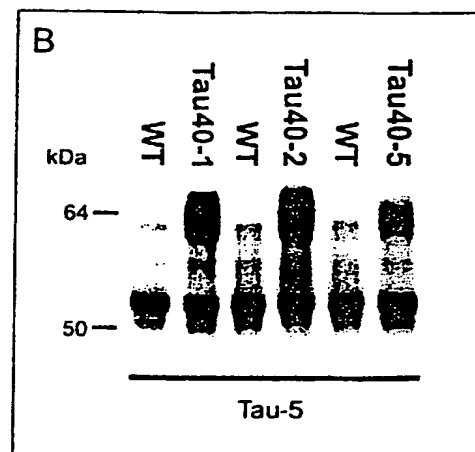
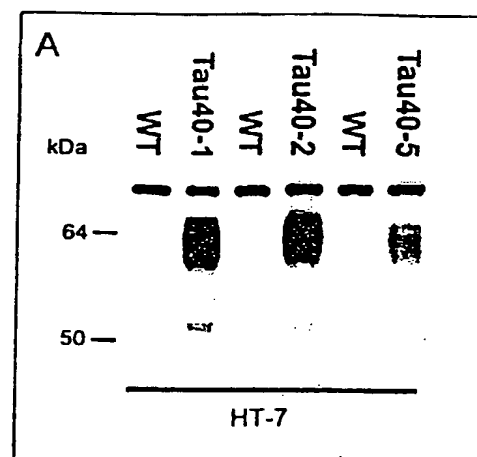


FIG. 3.



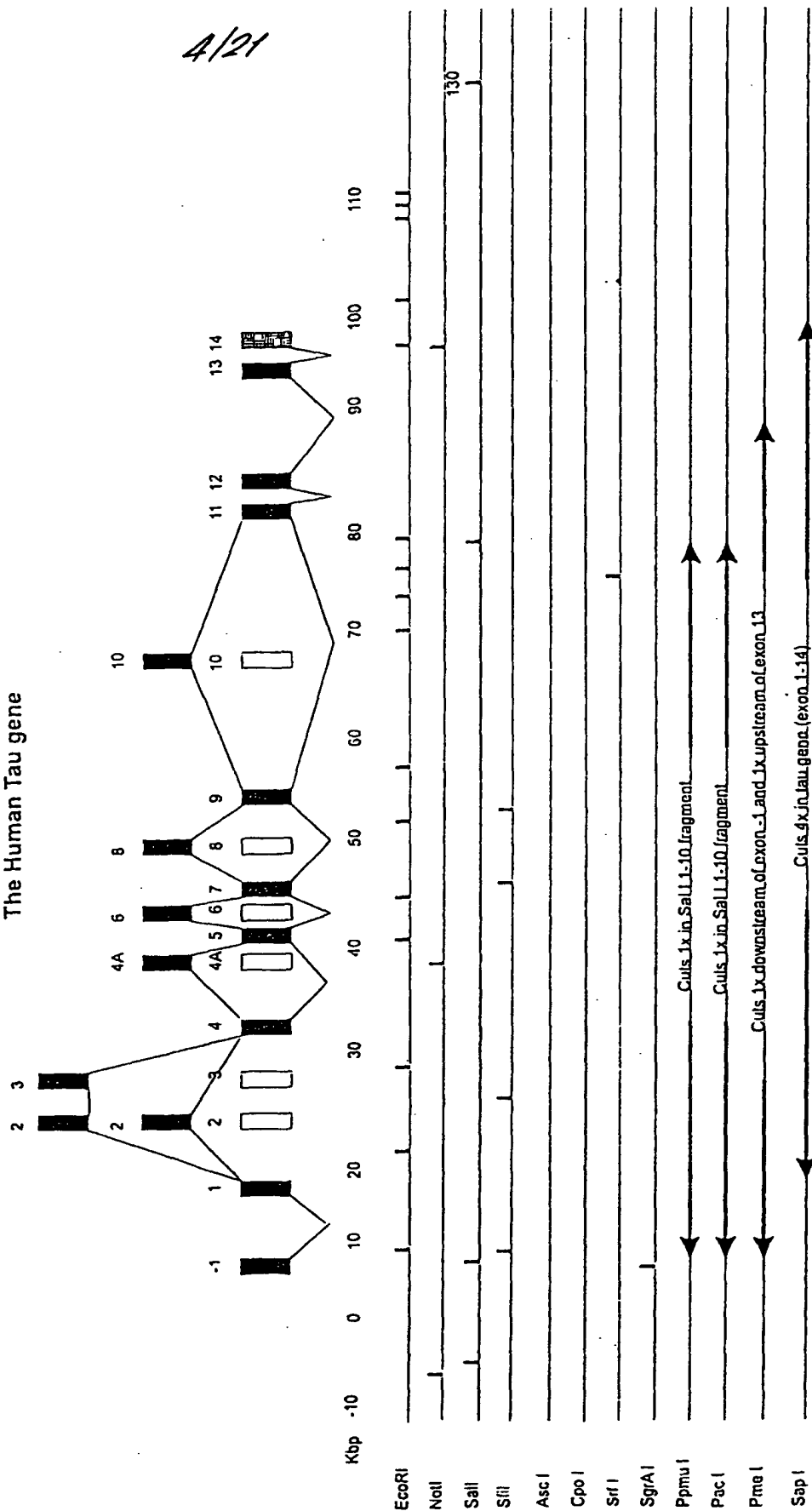
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FIG. 4.



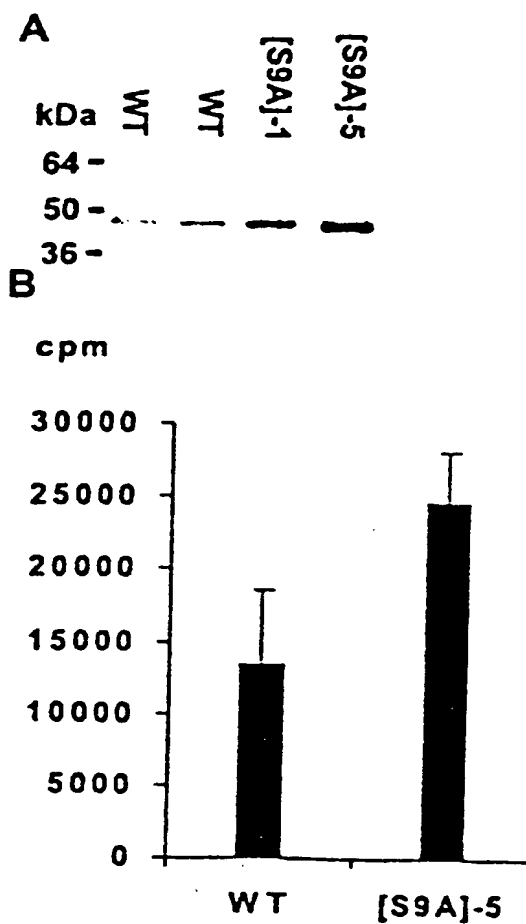
FIG. 5.

The Human Tau gene



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FIG. 6.



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FIG. 7

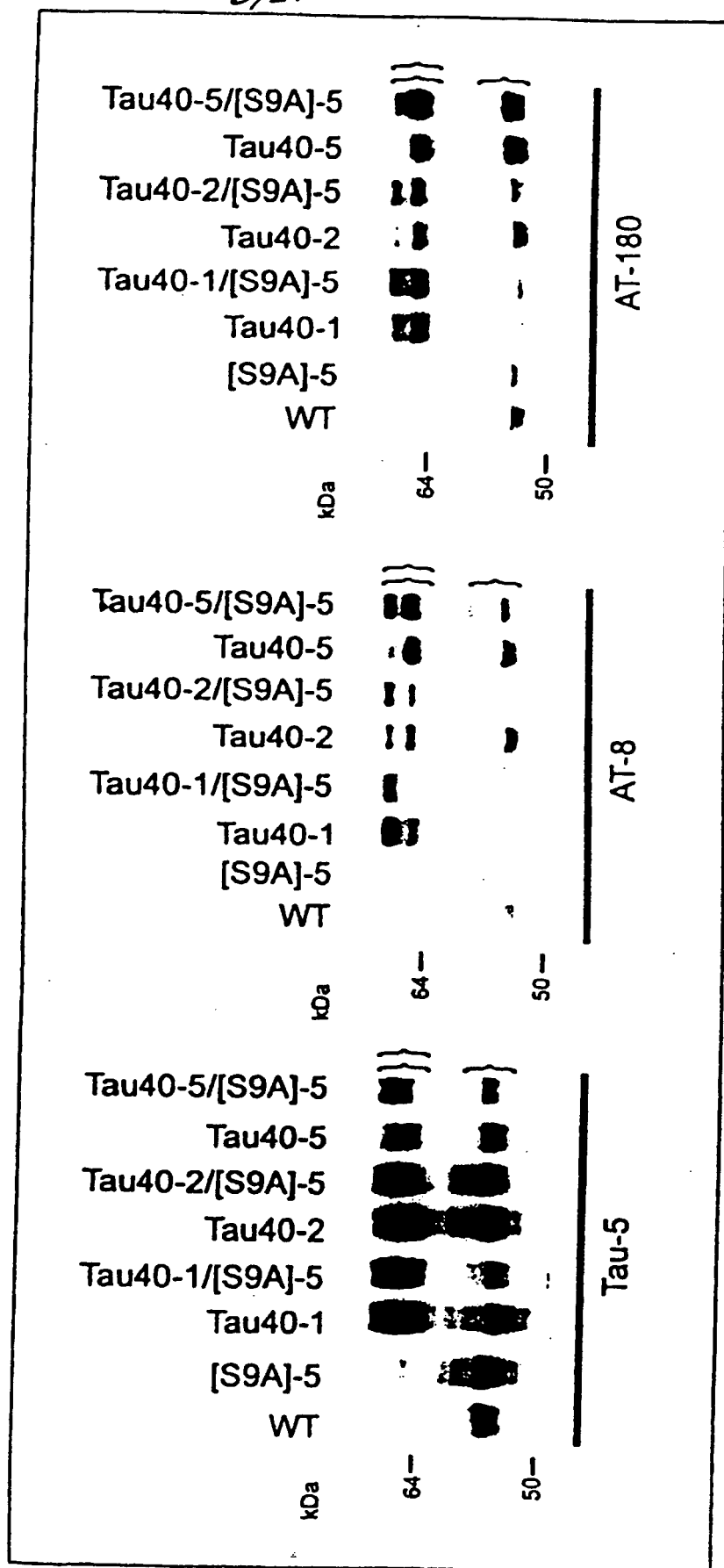
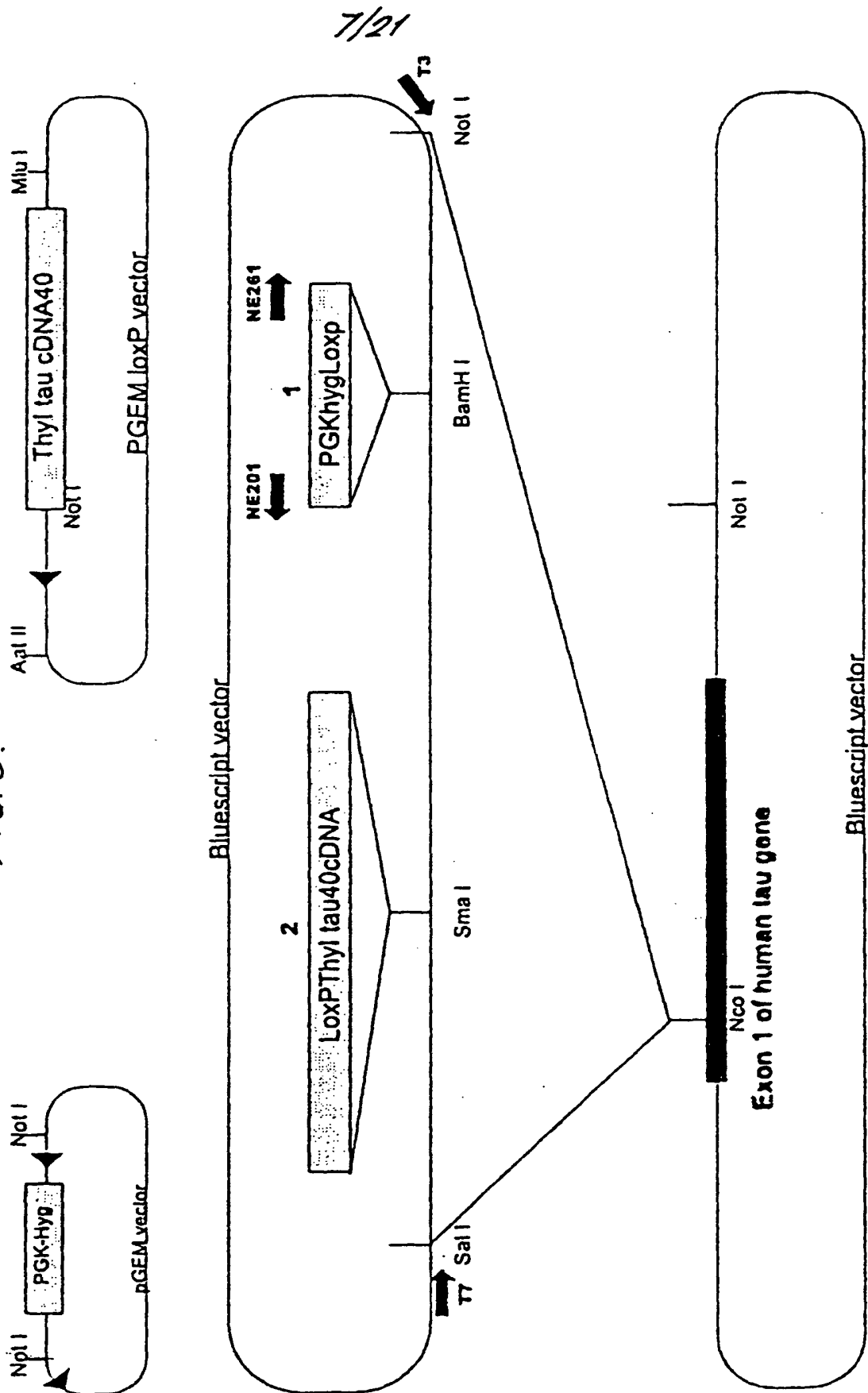
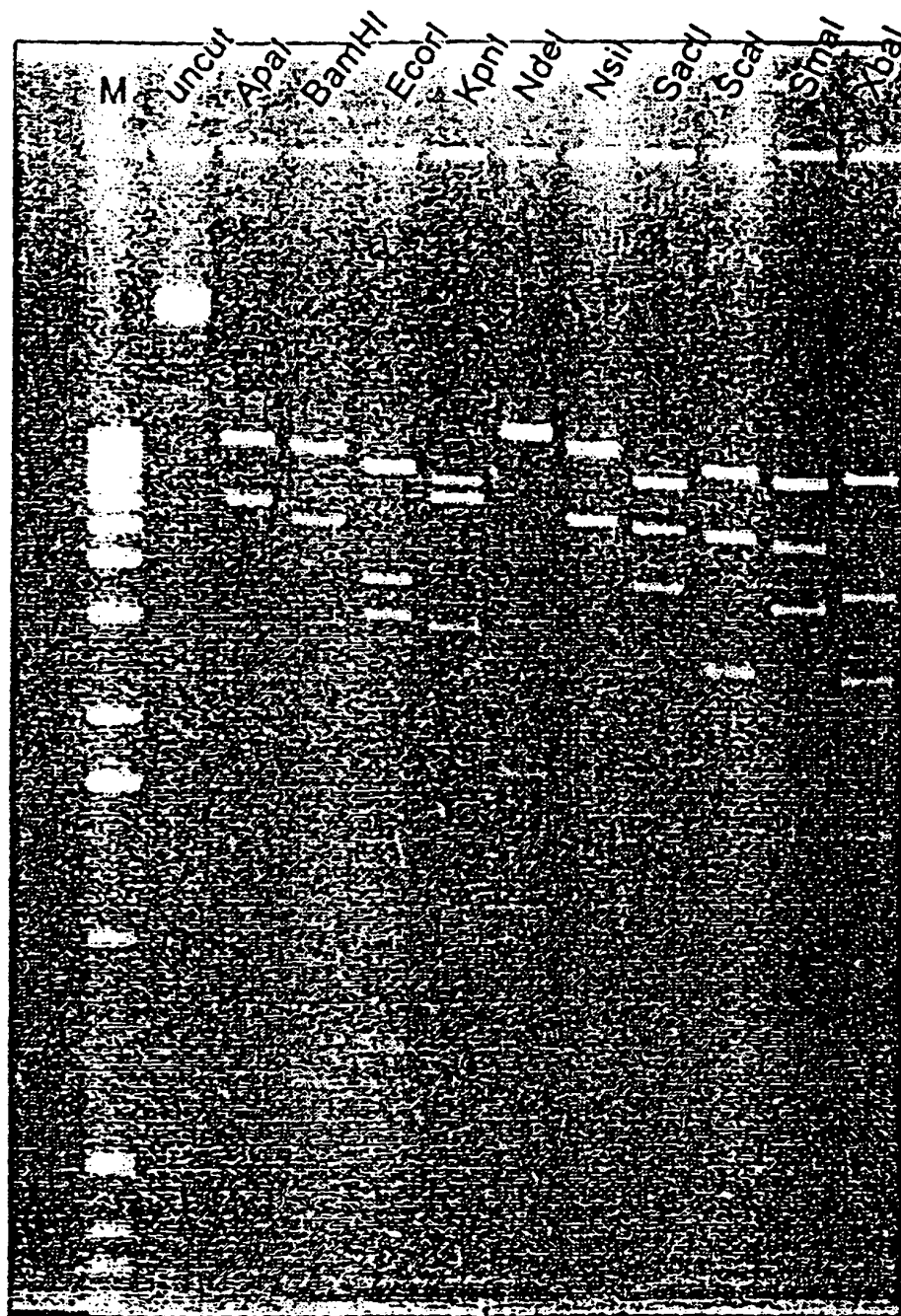


FIG. 8.

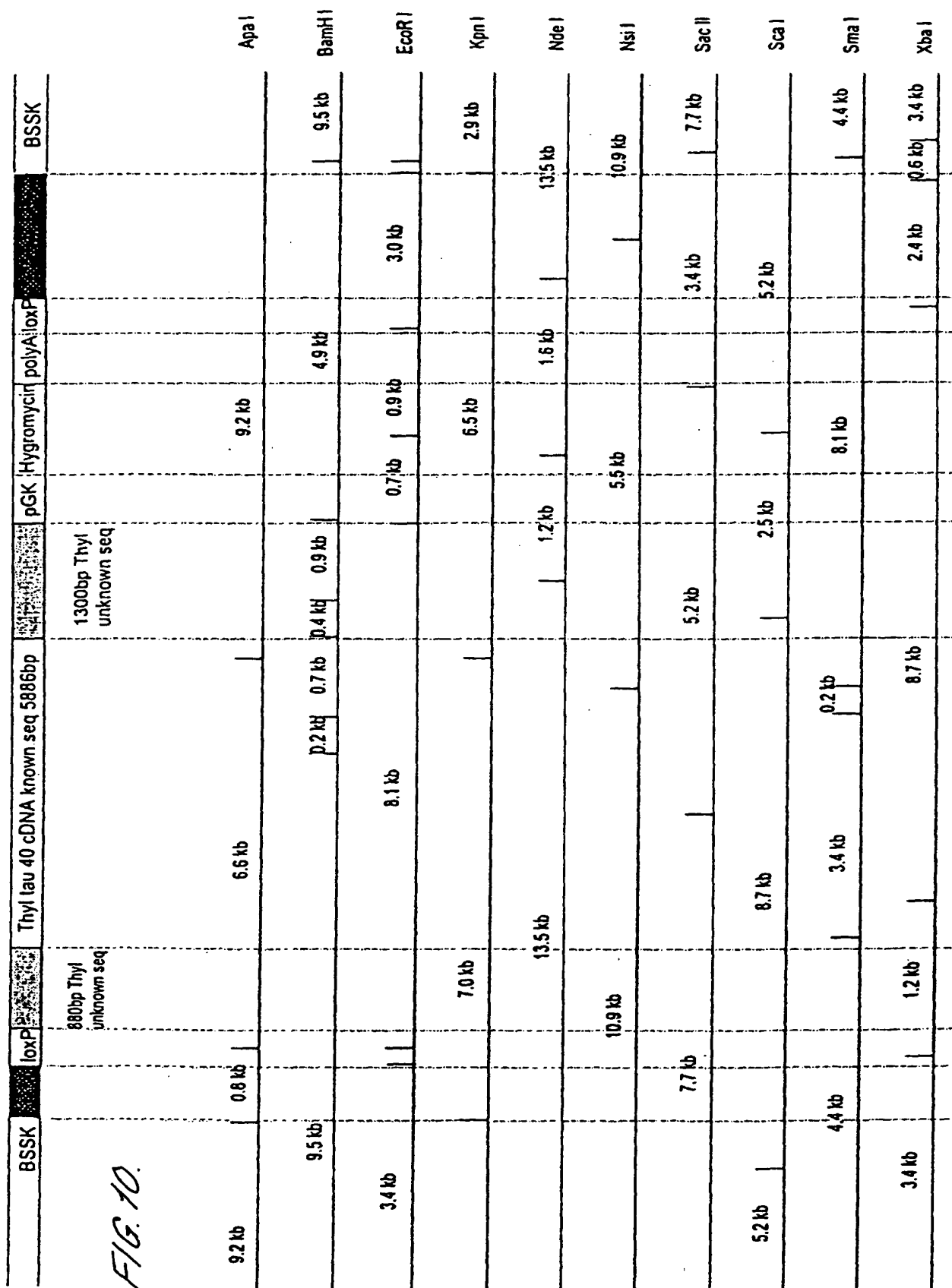


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FIG. 9.

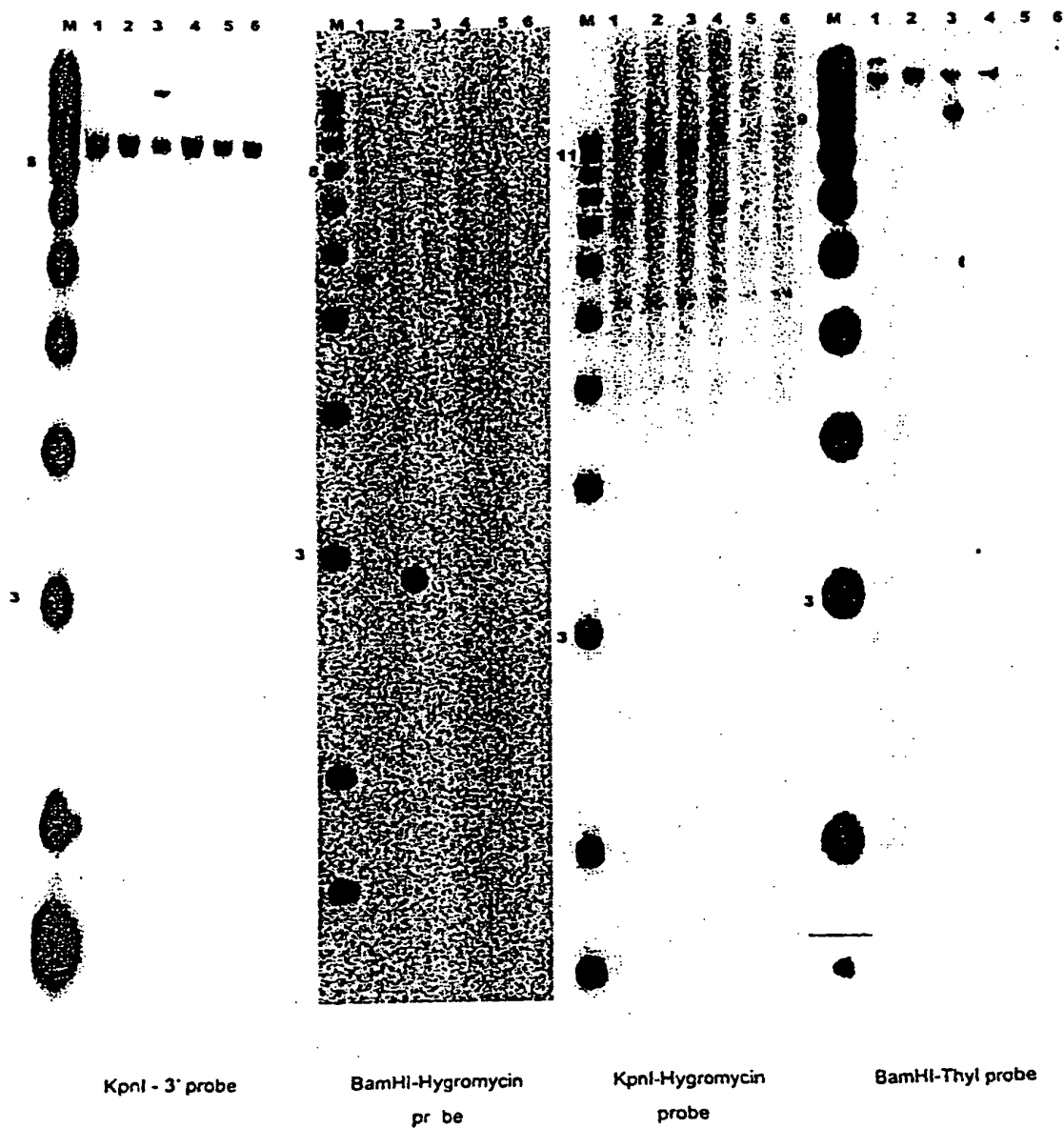


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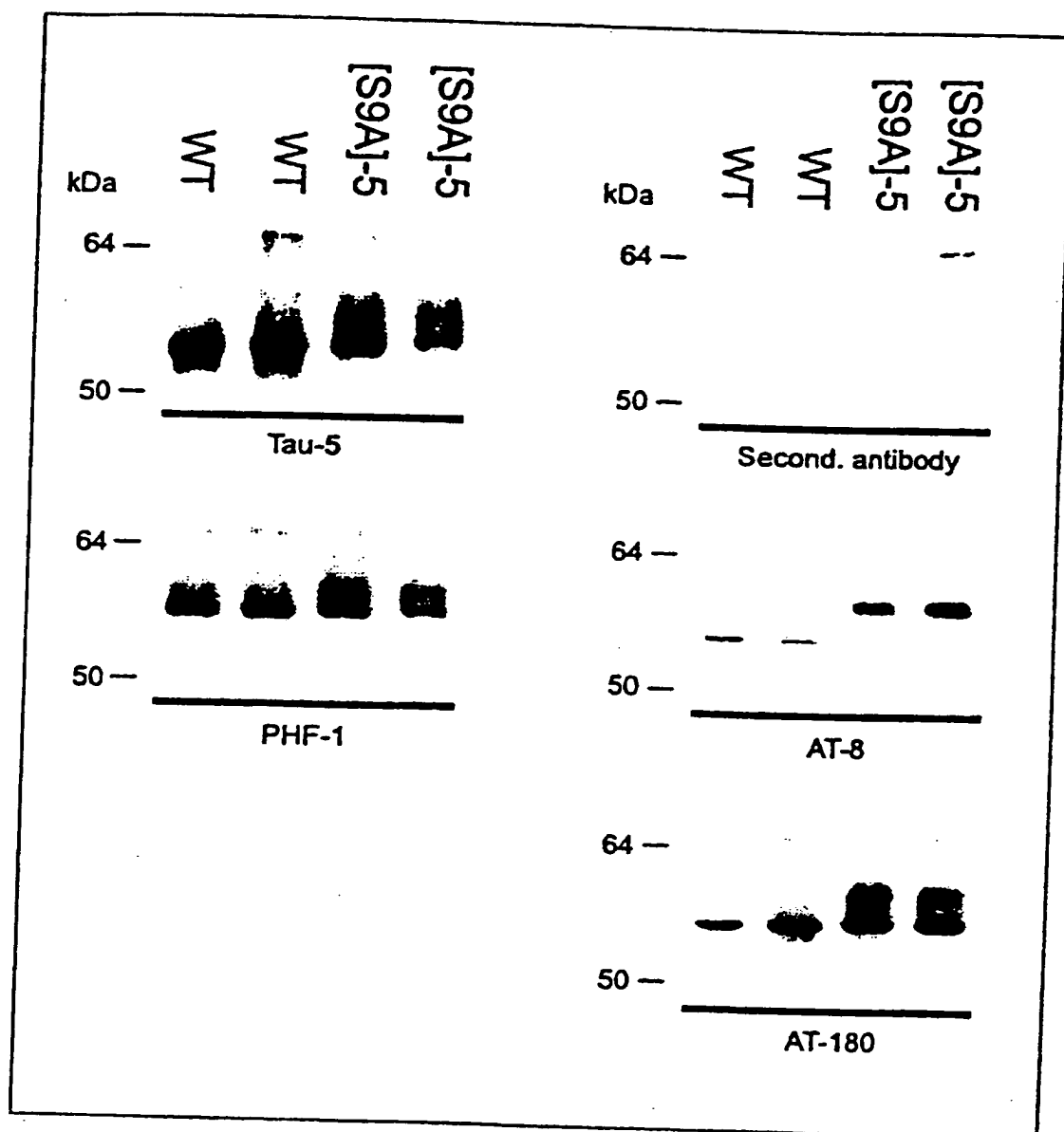
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FIG. 11.



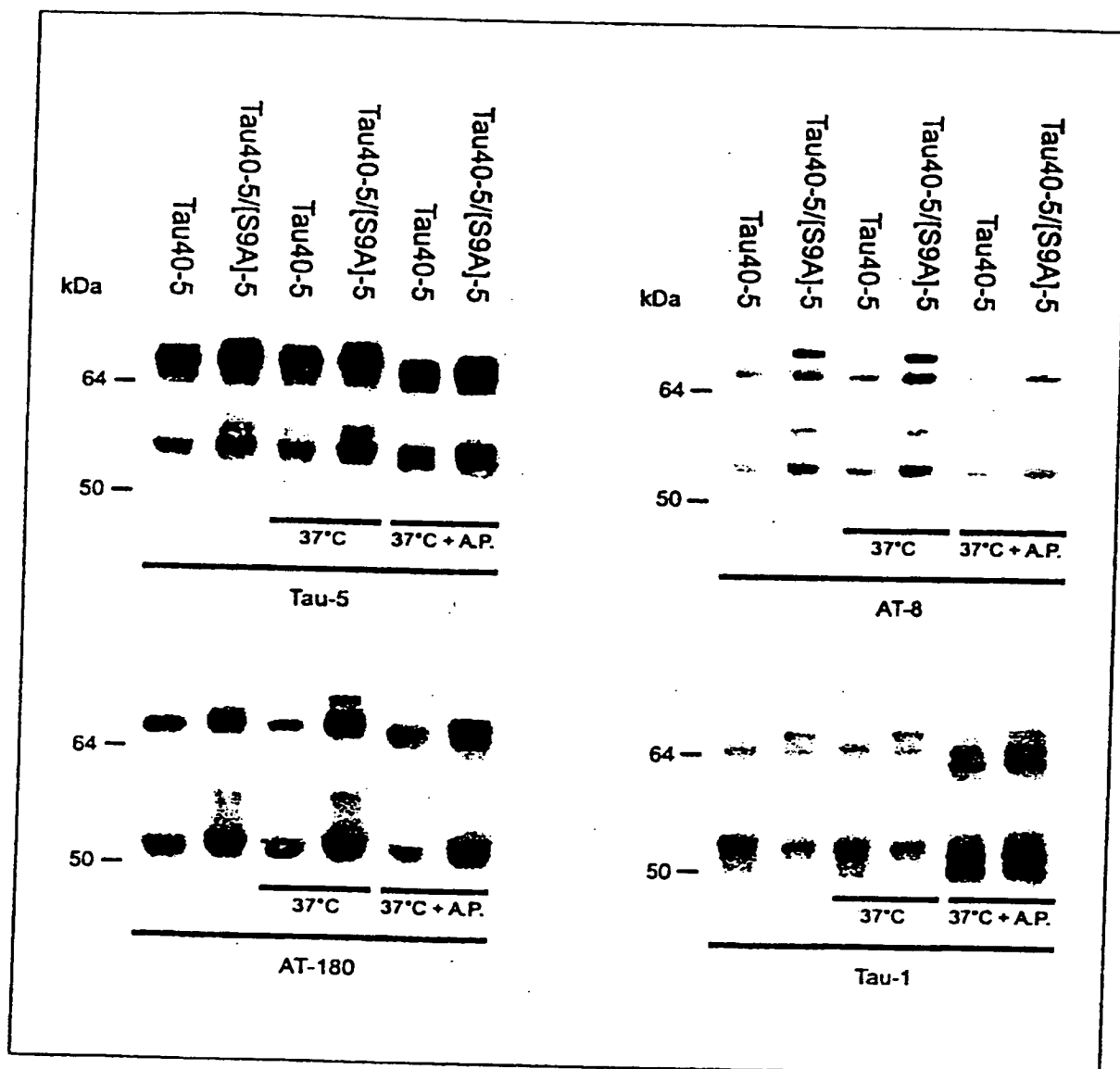
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FIG. 12.



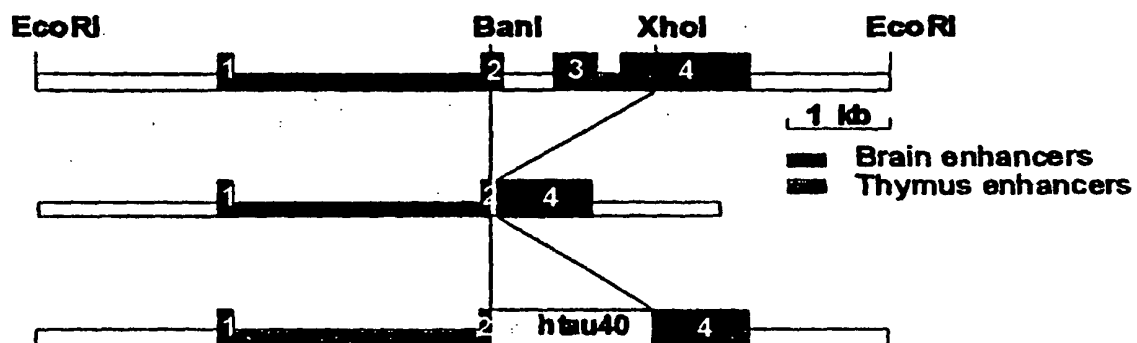
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FIG. 13.

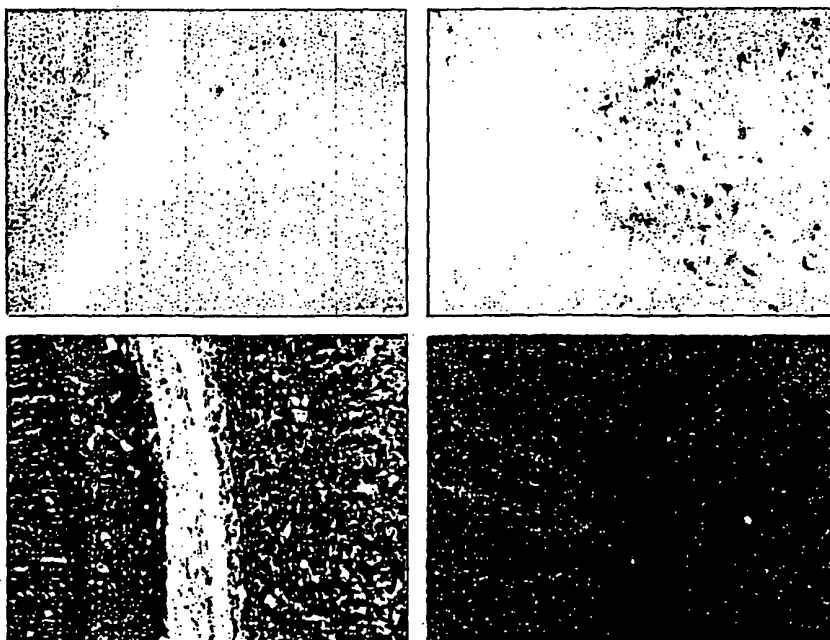
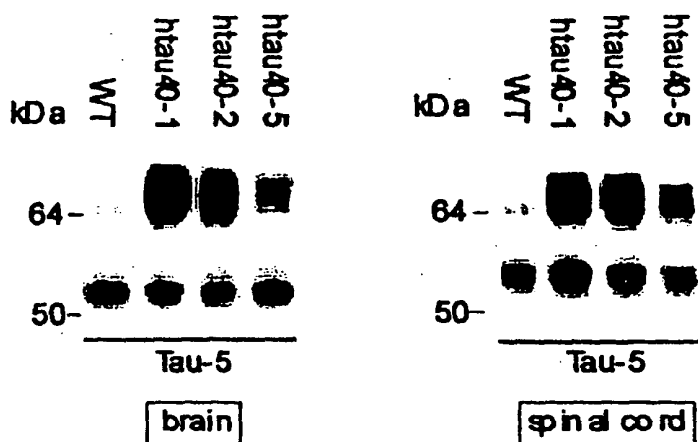


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FIG. 14.

(e)



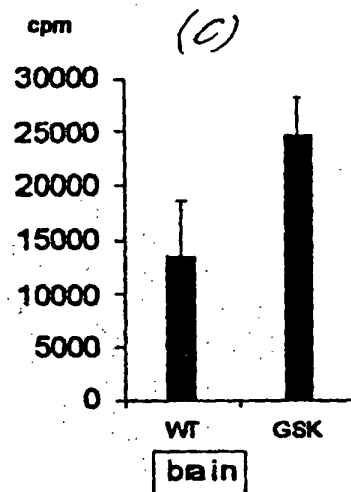
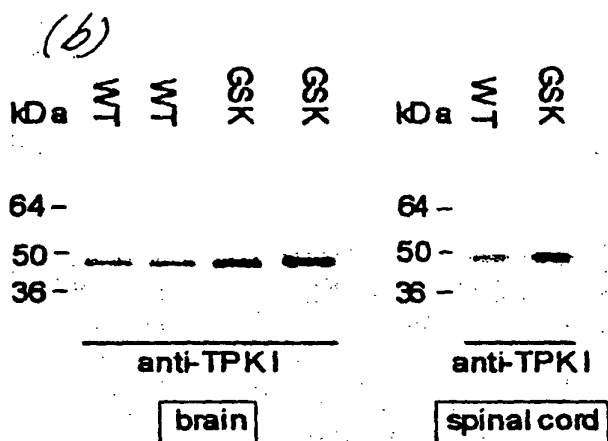
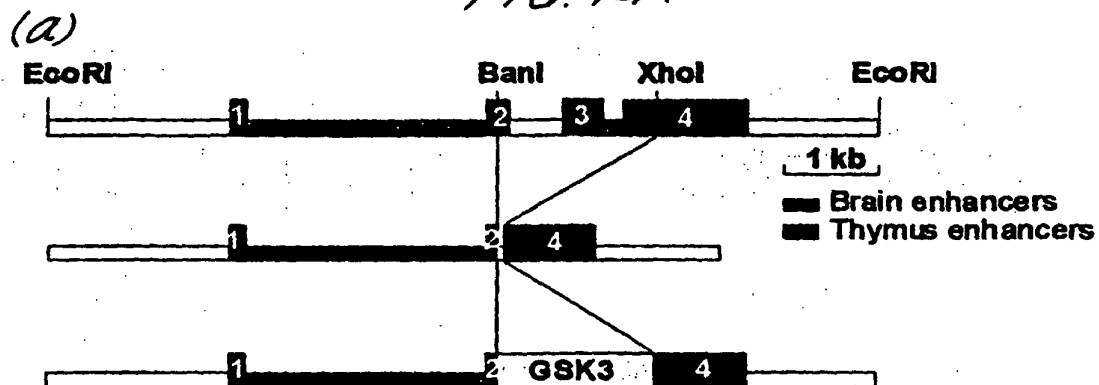
(f)



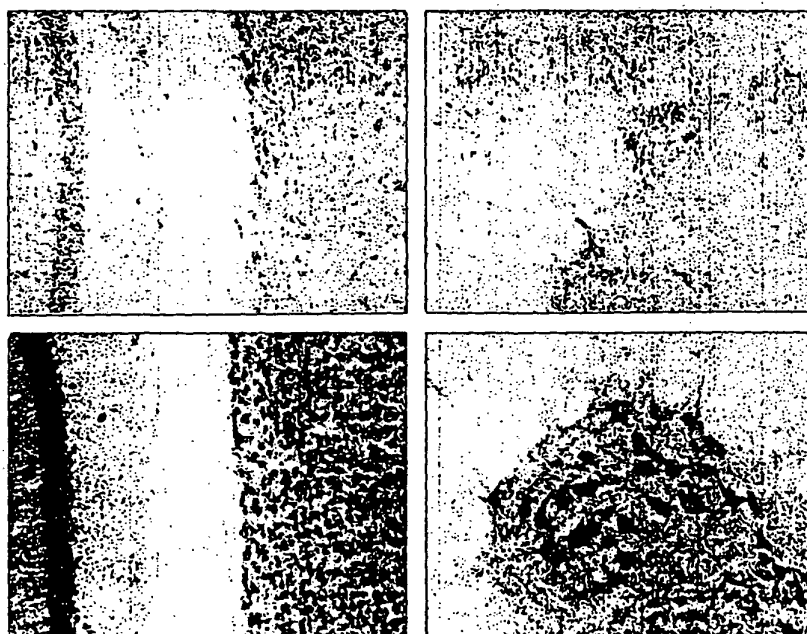
(g)

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FIG. 14.

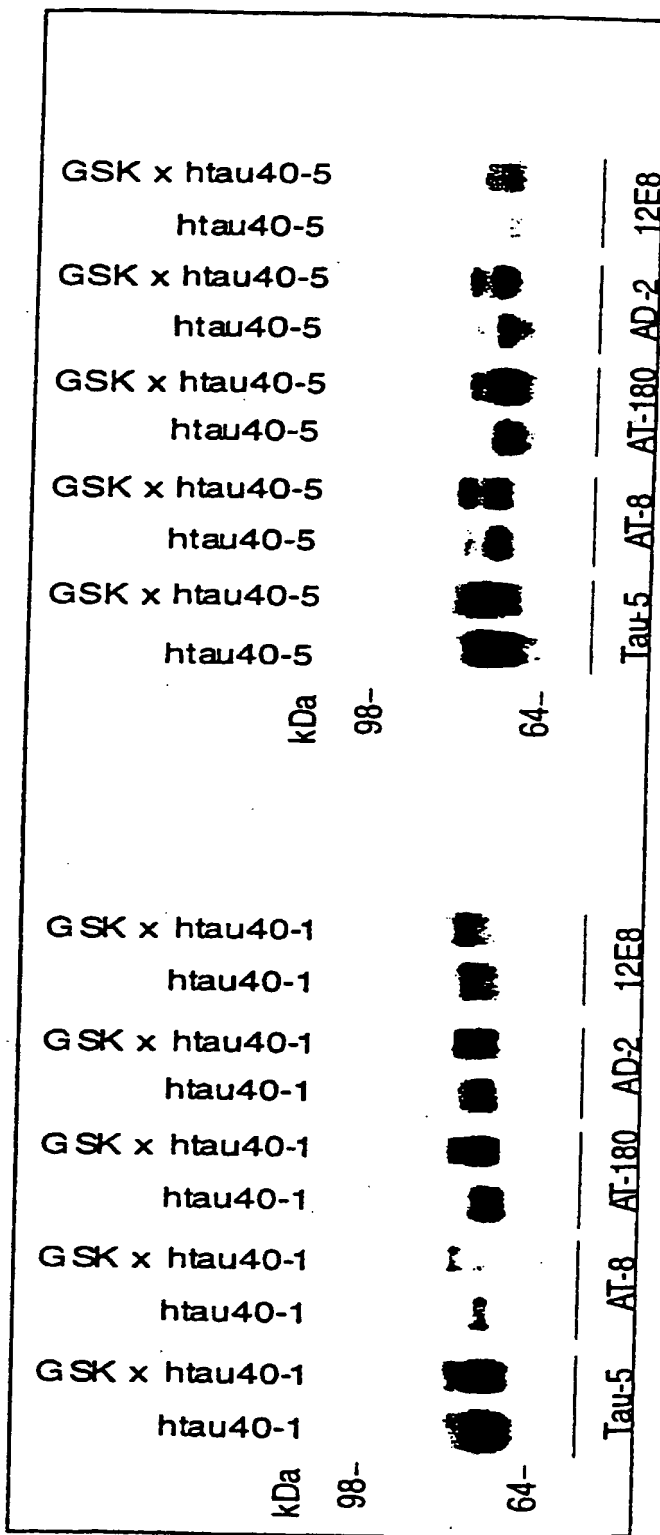


(d)



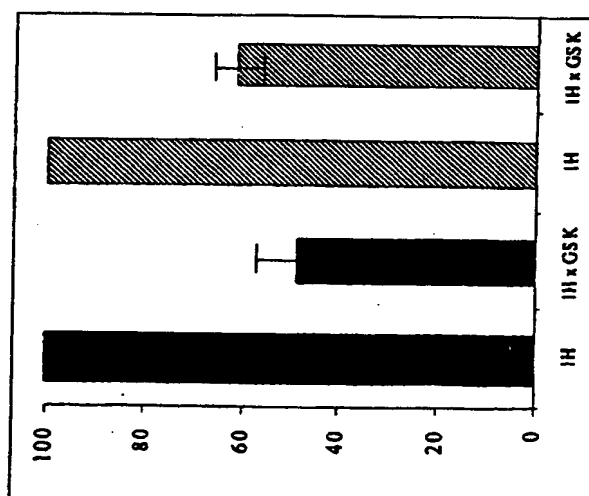
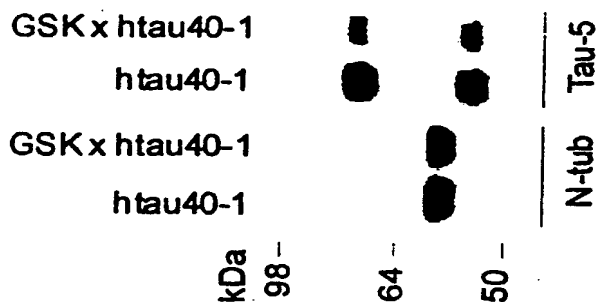
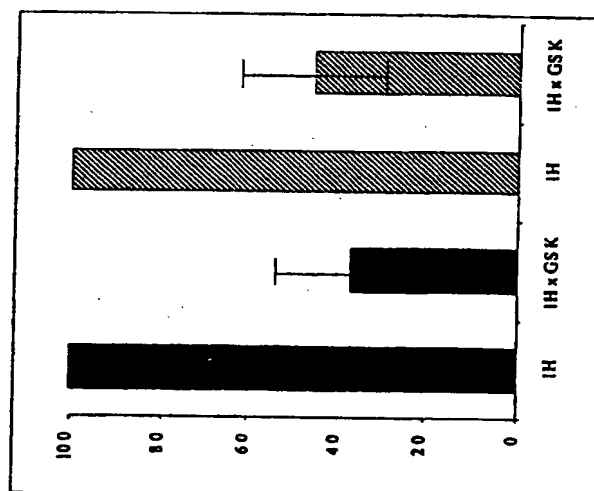
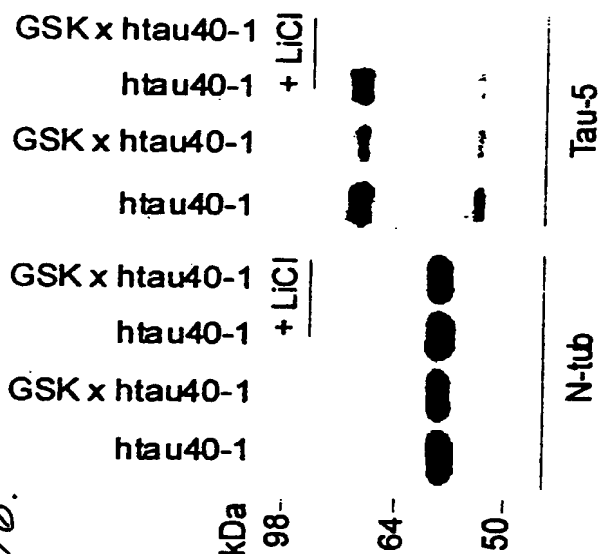
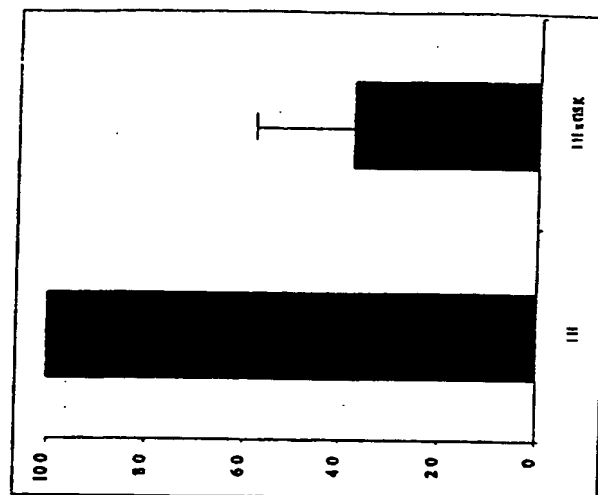
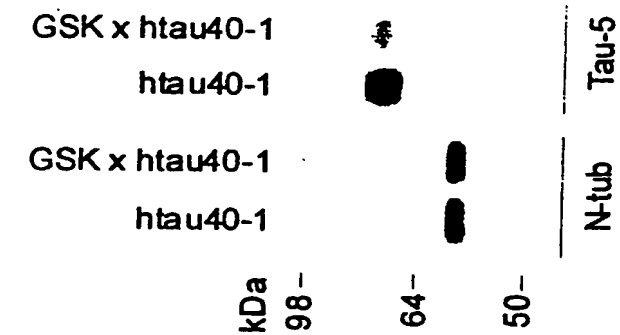
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FIG. 15.



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FIG. 16.



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FIG. 17

GSK x htau40-1
htau40-1

GSK x htau40-1
htau40-1

GSK x htau40-1
htau40-1

GSK x htau40-1
htau40-1

GSK x htau40-1
htau40-1

GSK x htau40-1
htau40-1

GSK x htau40-1
htau40-1

kDa

98 -

64 -

50 -

12E8

PHF-1

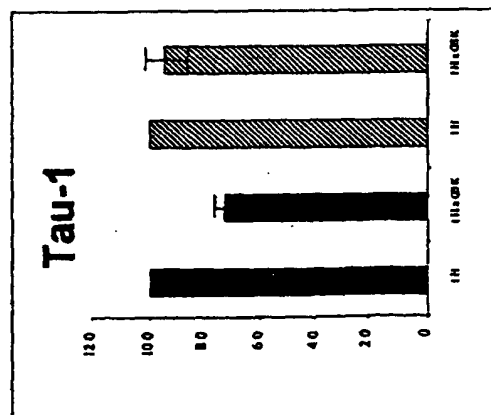
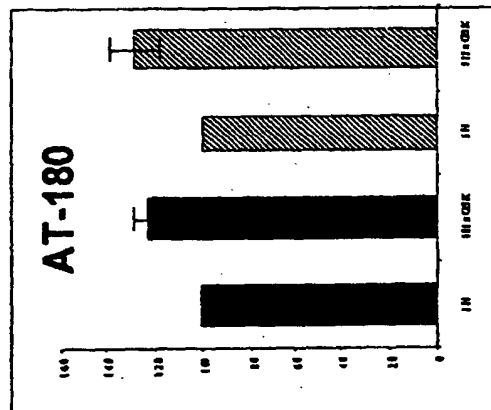
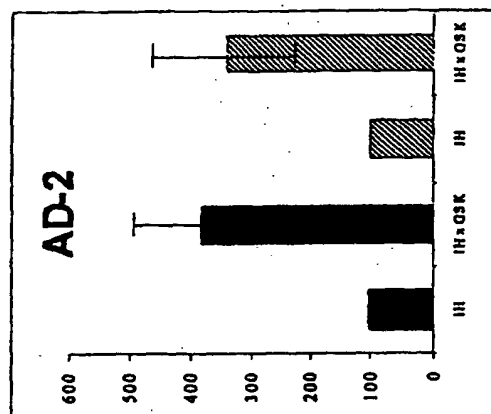
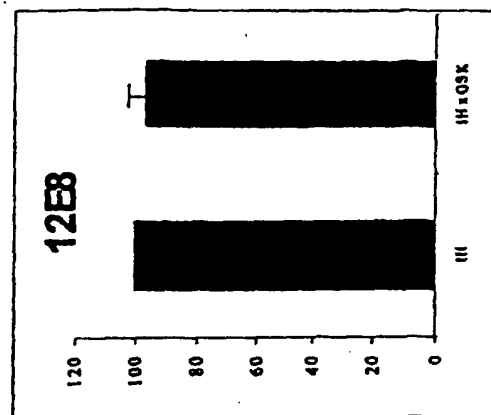
AD-2

AT-180

Tau-1

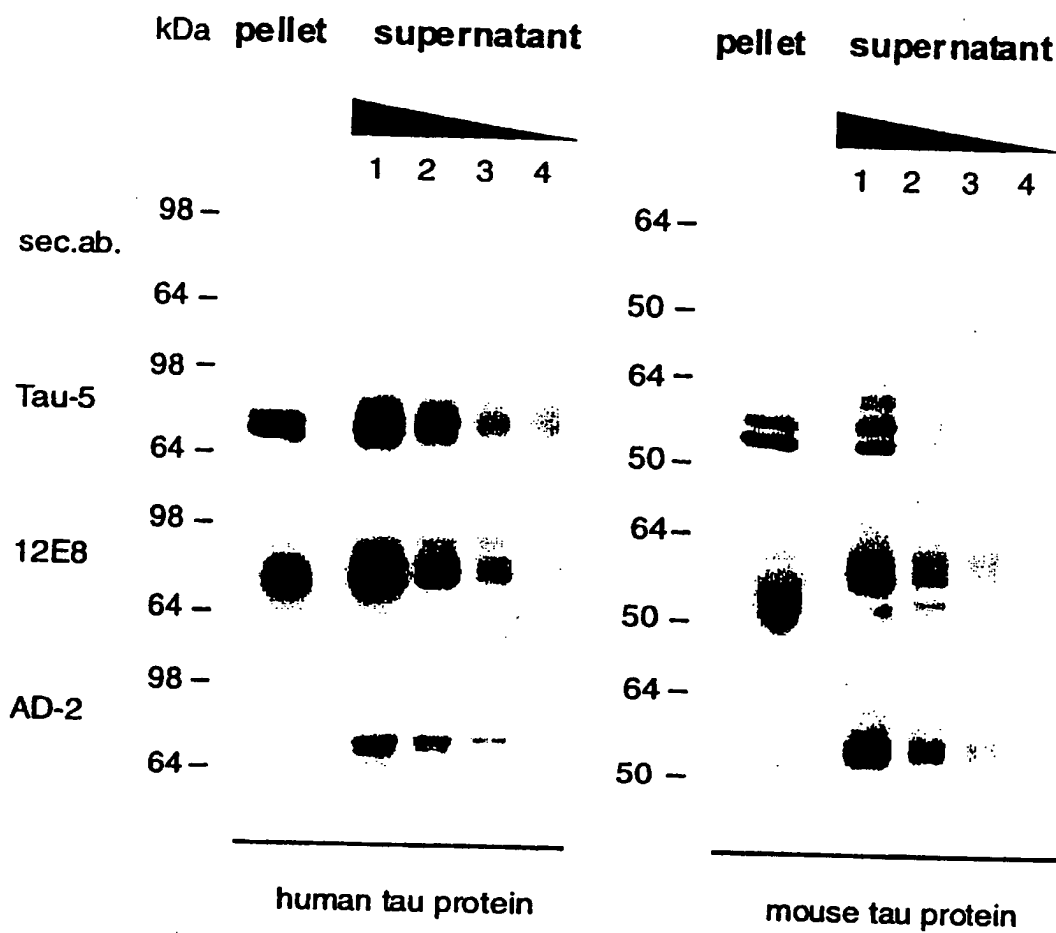
Tau-5

sec.ab.



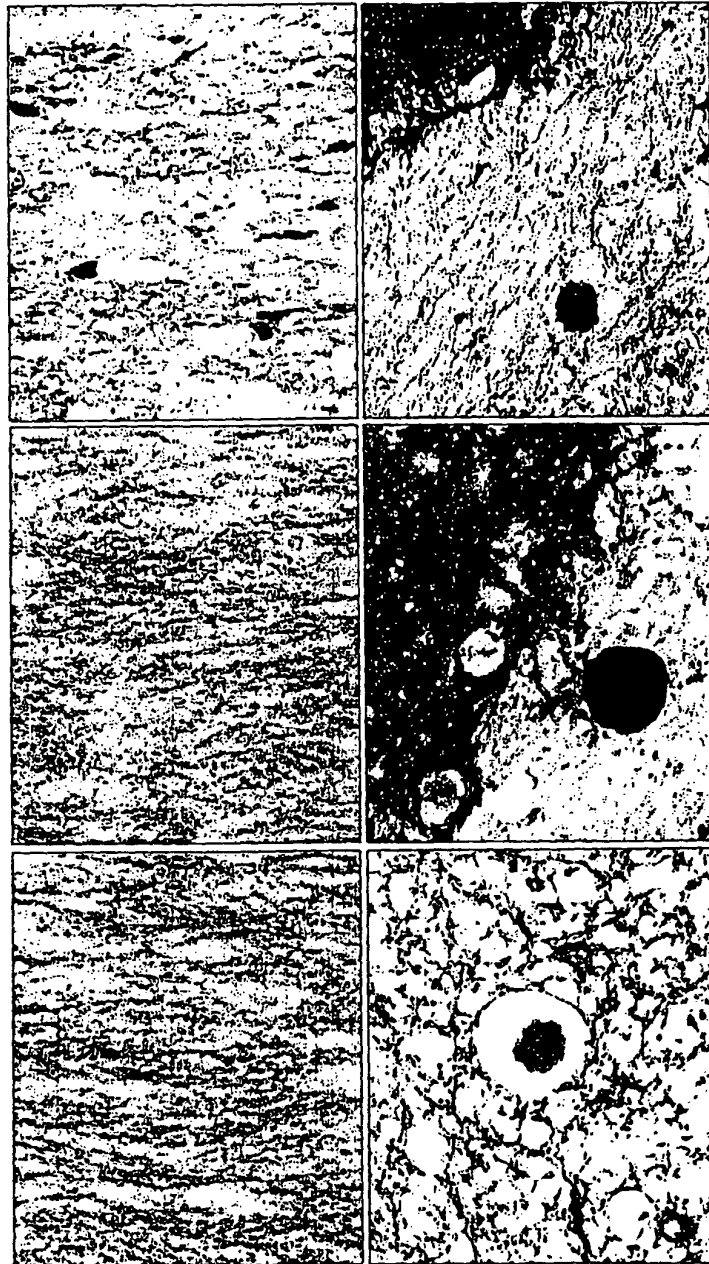
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FIG. 18.



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FIG. 19.



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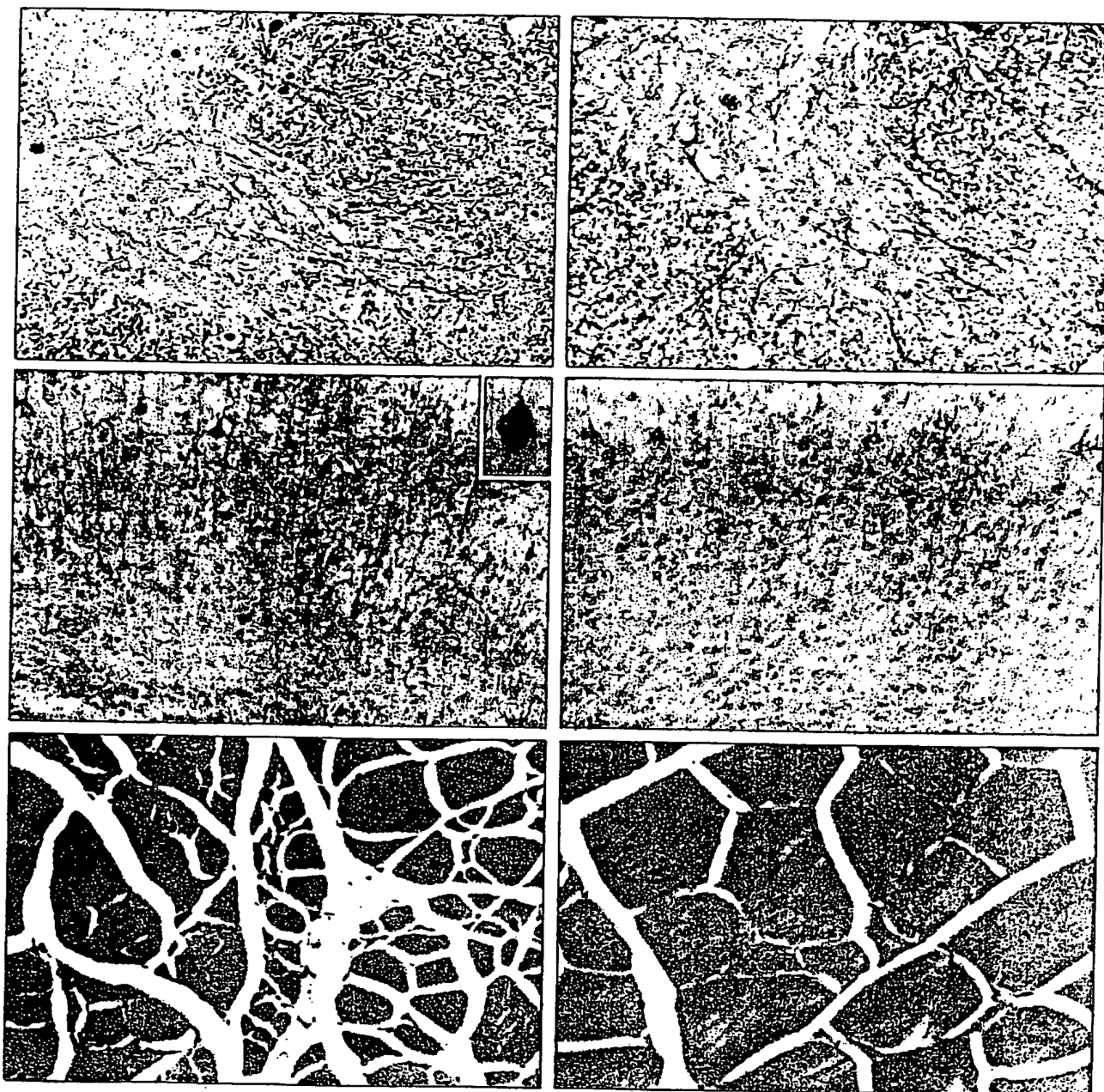


FIG. 20.

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FIG. 21.

